CLAIMS

What is claimed is:

1. An isolated nucleic acid encoding a eukaryotic *SIP1*, and any mutants, derivatives, variants, and fragments thereof.

2. The isolated nucleic acid of claim 1, wherein said nucleic acid shares at least about 20% homology with at least one of *huSIP1* (SEQ ID NO:1) and *XeSIP1* (SEQ ID NO:3).

3. The isolated nucleic acid of claim 2, wherein said nucleic acid is selected from the group consisting of (SEQ ID NO:1), and (SEQ ID NO:3).

4. An isolated nucleic acid encoding a eukaryotic SIP1, wherein said SIP1 shares at least about 20% homology with at least one of huSIP1 (SEQ ID NO:2), and XeSIP1 (SEQ ID NO:4), and any mutants, derivatives, variants, and fragments thereof.

5. An isolated polypeptide comprising a eukaryotic SIP1, and any mutants, derivatives, variants, and fragments thereof.

6. The isolated polypeptide of claim 5, wherein said SIP1 shares at least about 20% homology with at least one of SEQ ID NO:2 and SEQ ID NO: 4.

7. The isolated polypeptide of claim 6, wherein the amino acid sequence of said SIP1 is at least one of SEQ ID NO:2 and SEQ ID NO:4.

8. The isolated nucleic acid of claim 1, said nucleic acid further comprising a nucleic acid encoding a tag polypeptide covalently linked thereto.

9. The isolated nucleic acid of claim 8, wherein said tag polypeptide is selected from the group consisting of a myc tag polypeptide, a myc-pyruvate kinase tag polypeptide, a His6 tag polypeptide, an influenza virus hemagglutinin tag polypeptide, a maltose binding protein tag polypeptide, and a glutathione-S-transferase tag polypeptide.

10. The isolated nucleic acid of claim 1, said nucleic acid further comprising a nucleic acid encoding a promoter/regulatory sequence operably linked thereto.

11. The isolated nucleic acid of claim 10, said nucleic acid further comprising said nucleic acid of claim 9 encoding a tag polypeptide.

12. A cell comprising the nucleic acid of claim 11.

13. The cell of claim 12, wherein said cell is a DT40 cell.

14. A vector comprising the isolated nucleic acid of claim 1.

15. The vector of claim 14, said vector further comprising a nucleic acid encoding a promoter/regulatory sequence operably linked thereto.

16. A recombinant cell comprising the isolated nucleic acid of claim 1.

17. A recombinant cell comprising the vector of claim 14.

18. An antisense isolated nucleic acid complementary to the nucleic acid of claim 1.

19. A cell comprising the antisense nucleic acid of claim 18.

20. An antibody that specifically binds to a eukaryotic SIP1

polypeptide, or a fragment thereof.

21. The antibody of claim 20, wherein said antibody is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, and a synthetic antibody.

22. The antibody of claim 21, wherein said antibody is a monoclonal antibody selected from the group consisting of 2S7 and 2E17.

23. An isolated nucleic acid encoding a mammalian *Gemin3*, and any mutants, derivatives, variants, and fragments thereof.

24. The isolated nucleic acid of claim 23, wherein said nucleic acid shares at least about 20% homology with human *Gemin3* (SEQ ID NO:7).

25. The isolated nucleic acid of claim 24, wherein said nucleic acid is SEQ ID NO:7.

26. An isolated nucleic acid encoding a mammalian Gemin3, wherein said Gemin3 shares at least about 20% homology with human Gemin3 (SEQ ID NO:8), and any mutants, derivatives, variants, and fragments thereof.

27. An isolated polypeptide comprising a mammalian Gemin3, and any mutants, derivatives, variants, and fragments thereof.

28. The isolated polypeptide of claim 27, wherein said Gemin3 shares at least about 20% homology with SEQ ID NO:8.

29. The isolated polypeptide of claim 28, wherein said Gemin3 is SEQ ID NO:8.

30. The isolated nucleic acid of claim 23, said nucleic acid further comprising a nucleic acid encoding a tag polypeptide covalently linked thereto.

31. The isolated nucleic acid of claim 30, wherein said tag polypeptide is selected from the group consisting of a myc tag polypeptide, a myc-pyruvate kinase tag polypeptide, a His6 tag polypeptide, an influenza virus hemagglutinin tag polypeptide, a maltose binding protein tag polypeptide, and a glutathione-S-transferase tag polypeptide.

32. The isolated nucleic acid of claim 23, said nucleic acid further comprising a nucleic acid encoding a promoter/regulatory sequence operably linked thereto.

33. A vector comprising the isolated nucleic acid of claim 23.

34. The vector of claim 33, said vector further comprising a nucleic acid encoding a promoter/regulatory sequence operably linked thereto.

35. A recombinant cell comprising the isolated nucleic acid of claim 23.

36. A recombinant cell comprising the vector of claim 30.

37. An antisense isolated nucleic acid complementary to the nucleic acid of claim 23.

38. A cell comprising the antisense nucleic acid of claim 37.

39. An antibody that specifically binds to a mammalian Gemin3 polypeptide, or a fragment thereof.

40. The antibody of claim 39, wherein said antibody is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, and a synthetic antibody.

41. The antibody of claim 40, wherein said antibody is a monoclonal antibody selected from the group consisting of 11G9 and 12H12.

42. An antibody that specifically binds to a eukaryotic Survival of Motor Neurons (SMN) polypeptide, or a fragment thereof.

43. The antibody of claim 42, wherein the SMN is human SMN and further wherein said antibody is monoclonal antibody 2B1.

44. The antibody of claim 42, wherein said SMN is chicken SMN.

45. The isolated nucleic acid of claim 1, wherein said nucleic acid comprises a mutation that affects binding of SIP1 with SMN.

46. An isolated nucleic acid encoding human SMN, wherein said nucleic acid comprises a mutation which mutation affects binding of SMN with at least one of another SMN protein, a Gemin3 protein, and an SIP1 protein.

47. An isolated nucleic acid encoding the human Survival of Motor Neurons (SMN) protein, wherein said nucleic acid comprises a mutation which mutation affects pre-mRNA splicing.

48. A cell comprising the isolated nucleic acid of claim 45.

49. The isolated nucleic acid of claim 1, said nucleic acid comprising a mutation which mutation affects binding of SIP1 with SMN.

50. A fusion protein comprising a tag polypeptide and at least a portion of an SMN protein.

51. The fusion protein of claim 50, wherein said tag polypeptide is selected from the group consisting of a myc tag polypeptide, a myc-pyruvate kinase tag polypeptide, a His 6 tag polypeptide, an influenza virus hemagglutinin tag polypeptide, a maltose binding tag polypeptide, and a glutathione-S-transferase tag polypeptide.

52. A fusion protein comprising a tag polypeptide and at least a portion of an SIP1 protein.

53. A fusion protein comprising a tag polypeptide and at least a portion of a Gemin3 protein.

54. A vector comprising a nucleic acid encoding human SMN wherein said nucleic acid comprises a mutation and further wherein said mutation affects SMN binding to at least one of another SMN protein, a Gemin3 protein, and an SIP1 protein.

55. A composition comprising an isolated purified SMN protein and a protein that binds specifically with SMN.

56. The composition of claim 55, wherein said protein that binds specifically with SMN is selected from at least one of another SMN protein, an SIP1 protein, a Gemin3 protein, and an Sm protein.

57. The composition of claim 56, said composition further comprising a ribonucleic acid.

58. A method of stimulating snRNP assembly, said method comprising contacting an extract comprising snRNP components with SMN, thereby stimulating snRNP assembly.

59. A mammalian cell comprising an exogenous SMN modulating sequence selected from the group consisting of a nucleic acid encoding SMN, an antisense nucleic acid complementary to a nucleic acid encoding SMN, and a ribozyme specific for ribonucleic acid encoding SMN, wherein said cell exhibits higher or lower levels of SMN protein compared with an otherwise identical cell which does not comprise said exogenous SMN modulating sequence.

60. The cell of claim 59, wherein said exogenous SMN modulating sequence is an antisense nucleic acid and further wherein said cell exhibits a lower level of SMN protein compared with an otherwise identical cell which does not comprise said antisense nucleic acid.

61. The cell of claim 59, wherein said cell further exhibits an altered growth characteristic compared with an otherwise identical cell which does not comprise said antisense nucleic acid.

62. The cell of claim 59, wherein said exogenous SMN modulating sequence is a nucleic acid encoding SMN wherein said nucleic acid encoding SMN is covalently linked to a nucleic acid encoding a HA tag polypeptide, and further wherein expression of said exogenous SMN modulating sequence inhibits expression of endogenous SMN.

63. A method of identifying a compound which affects the level of SMN expression in a cell, said method comprising contacting said cell with a test compound and comparing the level of SMN expression in said cell with the level of SMN expression in a otherwise identical cell which is not contacted with said test compound, wherein a higher or lower level of SMN expression in said cell contacted with said compound compared with the level of SMN expression in said otherwise identical cell which is not contacted with said compound is an indication that said compound affects the level of SMN protein in said cell.

64. The method of claim 63, wherein said compound increases the level of SMN expression in a cell.

65. The method of claim 63, wherein said cell is obtained from a SMA type I patient.

66. The cell of claim 65, wherein said cell is selected from the group consisting of a fibroblast and a lymphoblastoid cell.

67. A method of identifying a test compound which is a candidate SMA therapeutic, said method comprising contacting a cell with a test compound and comparing the level of SMN expression in said cell with the level of SMN expression in an otherwise identical cell which is not contacted with said test compound, wherein a lower level of SMN expression in said cell contacted with said test compound compared with the level of SMN expression in said otherwise identical cell which is not contacted with said test compound is an indication that said test compound is a candidate SMA therapeutic, thereby identifying a compound which is a candidate SMA therapeutic.

68. The method of claim 67, wherein said cell is obtained from a SMA type I patient.

69. The cell of claim 68, wherein said cell is selected from the group consisting of a fibroblast and a lymphoblastoid cell.

70. A method of identifying a compound which affects the level of SMN expression in a cell comprising an SMN modulating sequence, said method comprising contacting said cell with a test compound and comparing the level of SMN expression in said cell with the level of SMN expression in an otherwise identical cell which is not contacted with said test compound, wherein a higher or lower level of

SMN expression in said cell contacted with said compound compared with the level of SMN expression in said cell which is not contacted with said compound is an indication that said compound affects the level of SMN expression in said cell.

71. The method of claim 70, wherein said SMN modulating sequence is selected from the group consisting of an isolated nucleic acid encoding SMN, an antisense nucleic acid complementary to a nucleic acid encoding SMN, and a ribozyme specific for ribonucleic acid encoding SMN.

72. The method of claim 71, wherein said SMN modulating sequence is an antisense nucleic acid complementary to a nucleic acid encoding SMN.

73. A method of identifying a compound useful for the treatment of SMA, said method comprising contacting a cell comprising an antisense nucleic acid complementary to a nucleic acid encoding SMN with a test compound and comparing the level of SMN expression in said cell with the level of SMN expression in an otherwise dentical cell which is not contacted with said test compound, wherein a higher level of SMN expression in said cell contacted with said compound compared with the level of SMN expression in said cell which is not contacted with said compound is an indication that said compound is useful to treat SMA, thereby identifying a compound useful for the treatment of SMA.

74. A method of assessing whether a test compound affects binding of SMN with a protein that specifically binds with SMN, said method comprising

(a) making a first preparation comprising a surface having at least a portion of SMN bound thereon, said test compound, and a labeled protein that specifically binds with SMN;

(b) assessing the amount of said labeled protein bound with the surface in said first preparation; and

(c) comparing the amount of said labeled protein bound with the surface in said first preparation and the amount of labeled protein bound with the surface in an

otherwise identical preparation to which said test compound is not added,

whereby a difference between the amount of labeled protein bound with the surface in said first preparation and in said otherwise identical preparation is an indication that said test compound affects the binding of SMN with a protein that specifically binds with SMN.

75. The method of claim 74, wherein said protein that specifically binds with SMN is selected from the group consisting of another SMN protein, a SIP1 protein, a Gemin3 protein, a SmB protein, a SmB' protein, a SmD1 protein, a SmD2 protein, and a SmD3 protein.

76. A method of assessing whether a test compound is useful for treatment of SMA, said method comprising

(a) making a first preparation comprising a surface having at least a portion of SMN bound thereon, said test compound, and a labeled protein that specifically binds with SMN;

(b) assessing the amount of said labeled protein bound with the surface in said first preparation; and

(c) comparing the amount of said labeled protein bound with the surface in said first preparation and the amount of labeled protein bound with the surface in an otherwise identical preparation to which said test compound is not added,

whereby a lower amount of said labeled protein bound with the surface in said first preparation and in said otherwise identical preparation is an indication that said test compound is useful for treatment of SMA.

77. The method of claim 76, wherein said protein that specifically binds with SMN is selected from the group consisting of another SMN protein, a SIP1 protein, a Gemin3 protein, a SmB protein, a SmB' protein, a SmD1 protein, a SmD2 protein, and a SmD3 protein.

78. A method of enhancing splicing of mRNA, said method comprising

incubating an *in vitro* pre-mRNA processing extract in the presence of SMN, or any mutant, derivative, variant, and fragment thereof, thereby enhancing splicing of said mRNA.

79. A method of identifying a compound that affects pre-mRNA splicing, said method comprising incubating an extract capable of pre-mRNA splicing in the presence or absence of a test compound and comparing the level of pre-mRNA splicing in said extract in the presence of said test compound with the level of splicing of pre-mRNA in the absence of said test compound, wherein a higher or a lower level of pre-mRNA splicing in said extract in the presence of said test compound, compared with the level of pre-mRNA splicing in said extract in the absence of said test compound, is an indication that said test compound affects pre-mRNA splicing.

80. A method of identifying a test compound that is useful to treat SMA, said method comprising incubating an extract capable of pre-mRNA splicing in the presence or absence of a test compound and comparing the level of pre-mRNA splicing in said extract in the presence of said test compound with the level of splicing of pre-mRNA in the absence of said test compound, wherein a higher level of pre-mRNA splicing in said extract in the presence of said test compound, compared with the level of pre-mRNA splicing in said extract in the absence of said test compound, is an indication that said test compound is useful to treat SMA.

81. A method of identifying a compound that affects snRNP assembly, said method comprising incubating an extract capable of snRNP assembly in the presence or absence of a test compound and comparing the level of snRNP assembly in said extract in the presence of said test compound with the level of snRNP assembly in the absence of said test compound, wherein a higher or a lower level of snRNP assembly in said extract in the presence of said test compound, compared with the level of snRNP assembly in said extract in the absence of said test compound, is an indication that said test compound affects snRNP assembly.

82. A method of identifying a test compound that is useful to treat SMA, said method comprising incubating an extract capable of snRNP assembly in the presence or absence of a test compound and comparing the level of snRNP assembly in said extract in the presence of said test compound with the level of snRNP assembly in the absence of said test compound, wherein a higher level of snRNP assembly in said extract in the presence of said test compound, compared with the level of snRNP assembly in said extract in the absence of said test compound, is an indication that said test compound is useful to treat SMA.

83. A method of assessing the presence or degree of SMA in a mammal, said method comprising obtaining a biopsy comprising motor neurons from said mammal and assessing the number and morphology of gems in said motor neurons, wherein a lower number of gems in said motor neurons, compared with the number of gems in motor neurons obtained from an otherwise identical mammal which does not have SMA, is an indication that said mammal has SMA, and further wherein the absence of or the presence of a minimal number of gems in said mammal having SMA is directly related to the severity of said SMA in said mammal.

84. A method of assessing the presence or degree of SMA in a mammal, said method comprising comparing the level of binding of SMN obtained from said mammal to a protein that specifically binds with SMN with the level of binding of SMN wild type to an identical protein that specifically binds with SMN, wherein a lower level of binding of said SMN from said mammal to said protein that specifically binds with SMN compared with the level of binding of SMN wild type with said identical protein that specifically binds with SMN is an indication of the presence or degree of SMA in a mammal.

85. The method of claim 84, wherein said protein that specifically binds with SMN is selected from the group consisting of an SMN protein, an SIP1 protein, and a Gemin3 protein.

86. A knock-out targeting vector, said vector comprising a first nucleic acid portion encoding a sequence 5' of the open reading frame encoding SMN and a second nucleic acid portion encoding a nucleic acid sequence 3' of the open reading frame encoding SMN.

87. The knock-out targeting vector of claim 86, wherein said SMN is chicken SMN (SEQ ID NO:9).

88. The targeting vector of claim 87, said vector further comprising a nucleic acid encoding a selectable marker covalently linked thereto.

89. The vector of claim 88, wherein said first and second nucleic acid portions flank said nucleic acid encoding said selectable marker.

90. A recombinant cell comprising the knock-out targeting vector of claim 86.

91. The cell of claim 90, said cell further comprising a vector comprising an isolated nucleic acid encoding SMN.

92. The cell of claim 91, wherein said cell is a chicken pre-B lymphoid DT40 cell.

93. A method of identifying a compound that affects SMN expression in a cell, said method comprising contacting the cell of claim 87 with a test compound and comparing the level of SMN expression in said cell with the level of SMN expression in an otherwise identical cell which is not contacted with said test compound, wherein a higher or lower level of SMN expression in said cell contacted with said test compound compared with the level of SMN expression in said otherwise identical cell which is not contacted with said compound is an indication that said compound affects SMN expression in a cell, thereby identifying a compound that

affects SMN expression in a cell.

94. A method of identifying a compound that is useful to treat SMA, said method comprising contacting the cell of claim 87 with a test compound and comparing the level of SMN expression in said cell with the level of SMN expression in an otherwise identical cell which is not contacted with said test compound, wherein a higher level of SMN expression in said cell contacted with said test compound compared with the level of SMN expression in said otherwise identical cell which is not contacted with said compound is an indication that said compound increases SMN expression in a cell, thereby identifying a compound that is useful to treat SMA.

95. A method of identifying a compound useful for the treatment of SMA, said method comprising contacting the cell of claim 87 with a test compound and comparing the level of growth of said cell with the level of growth of an otherwise identical cell which is not contacted with said test compound, wherein a higher level of growth of said cell contacted with said compound compared with the level of growth of said cell which is not contacted with said compound is an indication that said compound is useful to treat SMA.

96. An isolated nucleic acid encoding a chicken SMN.

97. The nucleic acid of claim 96, wherein said nucleic acid shares at least about 20% homology with SEQ ID NO:9.

98. An isolated nucleic acid encoding chicken SMN, wherein said chicken SMN shares at least about 20% homology with SEQ ID NO:10.

99. An isolated polypeptide comprising chicken SMN.

100. The polypeptide of claim 99, wherein said SMN shares at least about 20% homology with SEQ ID NO:10.

101. The polypeptide of claim 100, wherein said SMN is SEQ ID NO:10.